

Histoplasmin Sensitivity In Mississippi— A New Boundary

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In northern Mississippi, infection with histoplasmosis is about three times as common as in the southern half of the State. This is especially true of the delta section in the northwest.

Results of a study to evaluate the significance of skin tests for systemic mycoses suggest that the northern part of Mississippi lies within the area of endemic histoplasmosis in the United States. The study more clearly defines the southern border of this area, which is usually described as the middle west or the Mississippi River Basin and as extending south through Tennessee. Mississippi to the south thus compares as a border State with Kansas to the west of the area of high prevalence, although the demarcation is more definite in Kansas. Christie (1) considered Mississippi a part of the endemic area when he reported high infection rates of over 55 percent whereas Palmer (2) considered the State to be south of the area of high prevalence.

Skin Test Reactions

In the present study, skin tests with histoplasmin, blastomycin, and coccidioidin were performed on 295 patients of the Mississippi State Sanatorium, the only tuberculosis sanatorium in Mississippi, during the period March 1951 to March 1952. Sixty-five of the group (22 percent) reacted positively to histoplasmin (see table).

In northern Mississippi, 31.5 percent of the patients tested were positive reactors to histoplasmin. In southern Mississippi, 12.8 percent

were positive. Only 0.7 percent (2 patients) reacted positively to blastomycin, and 0.7 percent reacted positively to coccidioidin.

Neither of the two positive reactors to blastomycin reacted to histoplasmin, but both reactors to coccidioidin had positive reactions to histoplasmin identical in size to the coccidioidin reactions. Both also gave a definite history of infection typical of coccidioidomycosis during residence in the San Joaquin Valley in California. The following statistical data, therefore, refer only to the histoplasmin test.

Geographic Variation

When all tests were plotted as to county of residence (see map), it was apparent that there was a significant geographic variation. County of residence was considered the one where patients had lived for 1 year prior to admission to the sanatorium.

For the purposes of the study, the State was divided into northern and southern Mississippi along an imaginary line at the Big Black River which flows east-west centrally into the Mississippi River. Below the Big Black River are the coastal plains. Above the river are the delta section of the northwest and the hills of northeastern Mississippi.

Of the 149 patients residing below the dividing line of the river, 19 (12.8 percent) were positive to histoplasmin. Above the river, 46 (31.5 percent) of the 146 persons tested were positive. This difference is statistically significant.

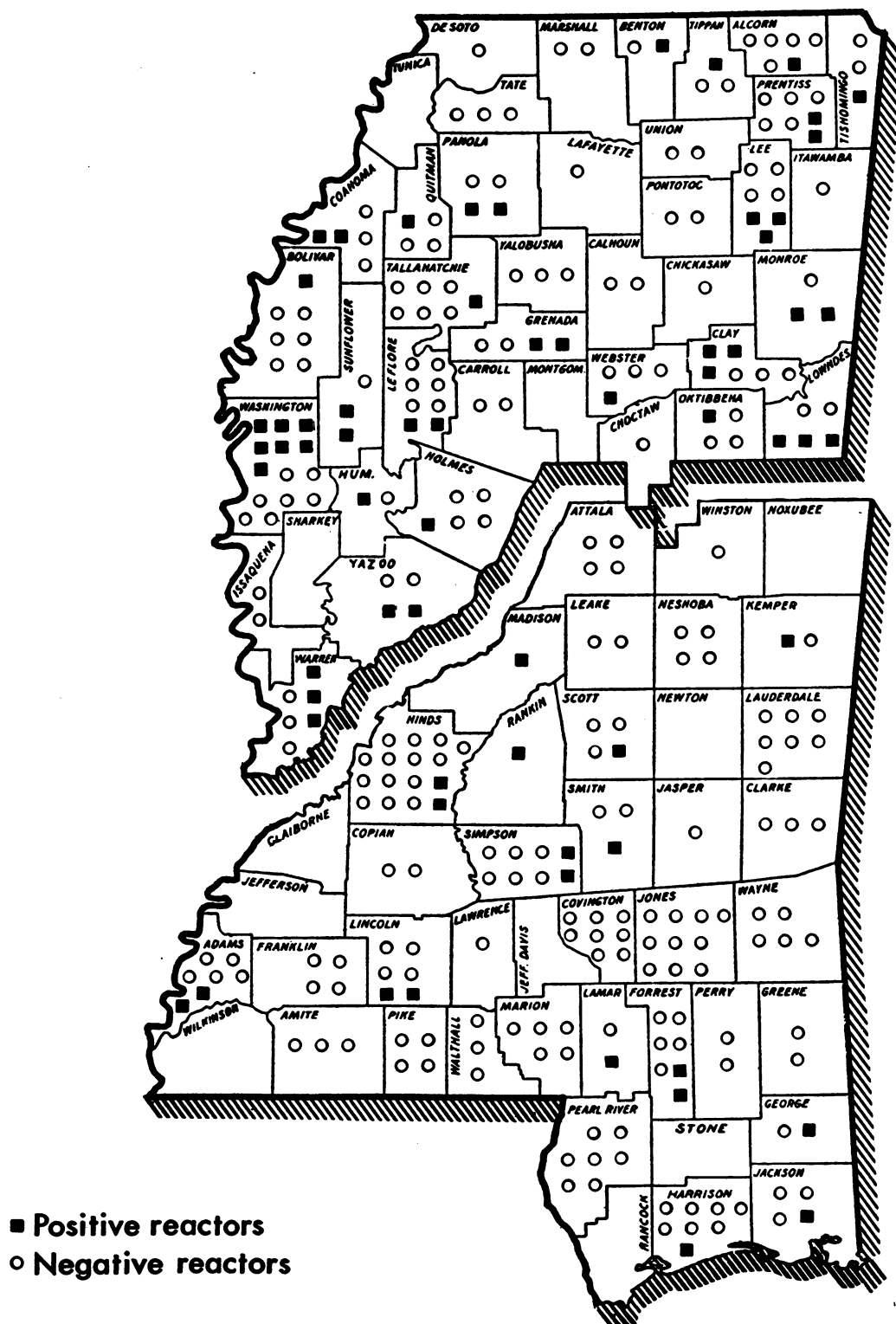
When the 13 counties in the delta section of northwestern Mississippi, the area of greatest prevalence, were considered apart from northern Mississippi, 61 tests were plotted for the area. Twenty-two (36.0 percent) were positive to histoplasmin. Our proven case of histoplasmosis (unreported) was from Bolivar County in the delta. It was not included in the skin tests because it was a diagnostic problem.

Materials and Methods

Blastomycin, coccidioidin, and histoplasmin concentrates were prepared each month in a sterile dilution of 1:1000 which was kept under refrigeration. New syringes were used and labeled for the respective antigens. One-tenth

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Geographic distribution of histoplasmin skin tests in northern and southern Mississippi



Results of histoplasmin skin tests in Mississippi

Item	Total	Sex		Race		Geographic division	
		Male	Female	White	Negro	Northern Mississippi	Southern Mississippi
Number of tests.....	295. 0	127. 0	168. 0	207. 0	88. 0	146. 0	149. 0
Percentage of reactors.....	22. 0	28. 3	17. 3	19. 8	25. 0	31. 5	12. 8
Standard deviation.....	2. 41	4. 00	2. 92	2. 77	4. 62	3. 84	2. 74
Difference.....		11. 0		5. 2		18. 7	

cubic centimeter of antigen was injected intradermally into the skin of the left forearm (histoplasmin), right forearm (blastomycin), and right upper arm (coccidioidin) simultaneously as suggested by Smith (3). Tests were read at 48 hours, and induration of 5 mm. or more was considered positive. Doubtful tests—there were only two—were considered negative.

The subjects were routine sanatorium admissions between 12 and 63 years, with an average age of 35.1 years. The age distribution in the northern and southern sections was not determined, and it is believed there could be little variance between the two samples. Age, however, was not considered in evaluating results because the percentage of histoplasmin sensitivity is highest in the young adult and middle age groups composing most sanatorium admissions (4, 5).

Critically ill patients were avoided because "critical illness exerts a depressing effect on skin sensitivity to tuberculin and histoplasmin" (6). Tests performed as diagnostic studies were excluded in an attempt to avoid sampling error.

Other Findings

Sex. Of the 127 men tested, 36 (28.3 percent) were positive to histoplasmin (see table). Of the 168 women, 29 (17.3 percent) were positive. This agrees with other studies which have determined that the rate of infection is slightly lower in women (5). The differences in this study are not statistically significant.

Race. Of the 207 white patients, 43 (19.8 percent) were positive. Of 88 Negro patients, 22 (25 percent) were positive. This differs from other studies in which the whites seemed to be more sensitive than the Negroes (5, 7), but the difference in rates is not statistically significant.

Statistical Significance

On the basis of the histoplasmin tests, the difference between the prevalence of reactors in northern Mississippi and those in the southern area is more than 2.5 times the standard deviation of the difference. Using this same level of significance, no significant difference between the Negro and white patients was demonstrated, and the difference between the sexes was of questionable significance.

NOTE: Blastomycin concentrate (B-8564) and histoplasmin concentrate (CT-189) were furnished by Eli Lilly & Co., Indianapolis. The coccidioidin (special dilution 1:10, lot 49028) was obtained from Cutter Laboratories, Berkeley, Calif.

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REFERENCES

- (1) Christie, A.: Histoplasmosis and pulmonary calcification. *Ann. New York Acad. Sc.* 50: 1283-1298 (1950).
- (2) Palmer, C. E.: Geographic differences in sensitivity to histoplasmin among student nurses. *Pub. Health Rep.* 61: 475-487 (1946).
- (3) Smith, D. T.: Fungous infection in the United States. *J.A.M.A.* 141: 1223-1226 (1949).
- (4) Furcolow, M. L., and Sitterley, J.: Further studies of the geography of histoplasmin sensitivity in Kansas and Missouri. *J. Kansas M. Soc.* 52: 584-589 (1951).
- (5) Furcolow, M. L., High, R. H., and Allen, M. F.: Some epidemiological aspects of sensitivity to histoplasmin and tuberculin. *Pub. Health Rep.* 61: 1132-1144 (1946).
- (6) Furcolow, M. L., Emge, M. E., and Bunnell, S. A.: Depression of tuberculin and histoplasmin sensitivity associated with critical illness. *Pub. Health Rep.* 63: 1290-1298 (1948).